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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,424	05/04/2005	Francis Fang	9626-2	9310

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,424	FANG ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-43 and 45-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-43 and 45-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-43, 45-63 are pending in this application.

Claim 44 is not listed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-43, 45-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The terms "aliphatic" "heteroaliphatic", "aryl", and "heteroaryl" are defined in the specification by examples. However, "[e]xemplification is not an explicit definition." The specification must set forth the definition explicitly and clearly, with reasonable clarity, deliberateness and precision, *Teleflex Inc. v. Ficosa North Am Corp.*, 63 USPQ2d 1374, (Fed. Cir. 2002), *Rexnord Corp. v. Laitram Corp.*, 60 USPQ2d 1854 (Fed. Cir. 2001).

The requirement of 35 USC 112, is not what is known or obvious to one of ordinary skill in the art but a "full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same", *Lookwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed Cir. 1997). See also the status above.

A claim must stand alone to define the invention, and incorporation into the claims by reference to the specification or an external source is not permitted. Ex parte Fressola, 27 USPQ 2d 1608, BdPatApp & Inter. (1993). Appropriate correction is required.

Claims 1-43, 45-63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for example VD-1207D, does not reasonably provide enablement for any other claimed compound, their utility as angiogenesis inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

"'In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, It is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the [compounds and the utilities] as obviously correct." *In re Jolles*, 628 F.2d 1327, 1332 (Fed. Cir. 1980), citing *In re Novak*, 306 F.2d 924 (CCPA 1962); see 340 F.2d 974, 977-78 (CCPA 1965).

"A specification disclosure which contains a teaching of the manner and process of making and using the invention . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), Id. at 1566, quoting *Marzocchi*, 439 F.2d 220, 223 (CCPA 1971); *Fiers v. Revel,* 984 F.2d 1164, 1171-72 (Fed. Cir. 1993), quoting *Marzocchi*, 439 F.2d at 223; see also *Armbruster*, 512 F.2d 676, 677 (CCPA 1975); *Knowlton*, 500 F.2d 566, 571 (CCPA 1974); *Bowen*, 492 F.2d 859 (CCPA 1974); *Hawkins*, 486 F.2d 569, 576 (CCPA 1973).

Where there is "no indication that one skilled in the art would accept without question [the instant compounds and method of use] and no evidence has been presented to demonstrate that the claimed products do have those effects *Novak*, 306 F.2d at 928, an applicant has failed to sufficiently demonstrate sufficient utility and therefore cannot establish enablement."' *In re Rasmusson,* 75 USPQ2d 1297 (CAFC 2005). The claimed invention is not enabled without undue experimentation for the following reasons:

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered. *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC, 1988): "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex prate Formal*, 230 USPQ 546. The breath of the claims includes all compounds of formula I. The compounds are numerous and are in the hundreds of thousands or millions. The substituents include all known "imines" "hydrazones", "amides" "anhydrides", "nitriles", "ketones", "acetals", "acyl halides", "aliphatics", "aryls", "heteroaryls", etc. The nature of the invention is using the compounds as pharmaceuticals. Applicant claims all the above substituents wherein aryl alone embraced mono and polycyclics of any number of rings and size. The specification discloses enablement for making only one example wherein none of the substituents is aryl.

While there are generic disclosures on how to perform modification of the process of making, none is directed to making a compound when the substituents are aryls or a compound where R2 and R3 together form cyclopropyl. Reference to other publications, such as Advanced

Organic Chemistry is made in the specification. But such are not incorporated by reference in accordance with the MPEP, which states as follows:

A mere reference to another application, publication or patent is not an incorporation of anything therein into the application containing such reference for the purpose of satisfying the requirement of 35 USC 112, first paragraph. *In re de Seversky,* 474 F.2d 671, 177 USPQ 144 (CCPA 1973). Particular attention should be directed to the subject matter and the specific portions of the referenced document where the subject matter being incorporated may be found. MPEP 608.01(p).

If the document is a pending US application: prior to allowance of an application that incorporates essential material by reference to a pending US application, if the referenced application has not been published or issued as a patent, applicant is required to amend the disclosure of the referencing application to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating the amendment consists of the same material incorporated by reference in the referencing application. MPEP 608.01(p).

In addition, the disclosures are too generic such that it is impossible to employ them in a process of making the claimed compounds. Example VD-1207D is not commensurate in scope with the claimed compounds. Steric hindrance and interference is more than likely to be a problem in making and using compounds having the claimed substituents. However, the specification fails to disclose how such problem could be overcome.

Hence, there is no absolute predictability or established correlation between the different substituents and the specification disclosure. The uncertainty presents one of ordinary skill in the art with obstacles and prevents her from accepting the invention on its face. The level of ordinary skill in pharmaceutical art is high but the level of unpredictability is very high.

The predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. In the instant invention, the amount of direction and guidance provided by applicant is limited to a single compound. There is no evidence in the specification that established nexus between the disclosure and the claims. *See Ex parte Mass*, 9 USPQ2d 1746, (1987).

Therefore, to make and use the instant invention, one of ordinary skill in the art would have to perform significant amount of experimentation to determine if in fact any compound having the various substituents can be made. Even then, there is no conclusive evidence such compounds would have the asserted utilities. The compounds must be made by trial and errors. Such is deemed undue experiment under the US patent practice.

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding any of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. By deleting the terms the rejection would be overcome.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-43, 45-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

For the reason set forth above under 35 USC 112, first paragraph, the claims are indefinite. It is not possible to ascertain the metes and bounds of the claims. Applicant must

show possession of the invention by describing it with all the claimed limitations. *Lookwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed Cir. 1997).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-6, 8, 10-15, 17-19, 22-24, 26-27, 29, 31-36, 38-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Genshi et al., JP 62-294619.

Genshi et al., disclose compounds and composition thereof as antitrichophytial agent wherein, R1 is ethyl or propyl, R9 is CH=NQ and Q is OH or optionally substituted amine. See the abstract and compounds of formula I.

The compounds of Genshi et al., have limited number of variations for each substituent, there are no alternative points of attachments of the substituents to the rings and the parent structural nuclei do not change. Therefore, Genshi "has described to those of ordinary skill in [the] art each of the various permutations involved here as fully as if he had drawn each structural formula or had written each name." *In re Petering,* 133 USPQ 275 (CCPA 1962), *Bristol-Myers Squibs Co. v. Benvenue Labs. Inc.*, 246 F3d 1368, 1380 (Fed Cir, 2001).

Claims 1-3, 5-6, 8, 10-19, 22-24, 26-27, 29, 31-40, 43, 45-46, 48-49, 51, 53-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Naruse et al., J. Antibiotics (2000), Vol. 53(6), pp. 579-590.

Naruse et al., disclose compounds A1-2, B1-2, C1-2, D, E1-3, G1-2, H, their compositions and method of use as angiogenesis inhibitors. See Fig. I, page 580.

Claims 1-3, 5, 8, 10, 12-19, 22-24, 26, 29, 31, 33-40, 43, 45-46, 48, 51, 53, 55-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Wakabayashi et al., WO 99/60000.

Wakabayashi et al., disclose compounds and composition thereof useful as neovascularization inhibitors wherein, R1 is lower alkoxy, R9 is H, aldehyde (CHO), lower acyl, R4 is lower alkyl. See the abstract and compounds of formula I.

The compounds of Wakabayashi et al., have limited number of variations for each substituent, there are no alternative points of attachments of the substituents to the rings and the parent structural nuclei do not change. Therefore, Wakabayashi "has described to those of ordinary skill in [the] art each of the various permutations involved here as fully as if he had drawn each structural formula or had written each name." *In re Petering,* 133 USPQ 275 (CCPA 1962), *Bristol-Myers Squibs Co. v. Benvenue Labs. Inc.*, 246 F3d 1368, 1380 (Fed Cir, 2001).

Claims 1-3, 5-6, 8, 10-19, 22-24, 26-27, 29, 31-39, 43, 45, 48-49, 51, 53-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Genshi et al., JP 61-190575.

Genshi et al., disclose compounds and composition thereof useful as antitumor agents wherein, R1 is H, R4 is H or OH and R9 is CHO. See the abstract and compounds of formula I.

The compounds of Genshi et al., have limited number of variations for each substituent, there are no alternative points of attachments of the substituents to the rings and the parent structural nuclei do not change. Therefore, Genshi "has described to those of ordinary skill in [the] art each of the various permutations involved here as fully as if he had drawn each structural formula or had written each name." *In re Petering,* 133 USPQ 275 (CCPA 1962), *Bristol-Myers Squibs Co. v. Benvenue Labs. Inc.*, 246 F3d 1368, 1380 (Fed Cir, 2001).

Claims 1-3, 5-6, 8, 10-19, 22-24, 26-27, 29, 31-39, are rejected under 35 U.S.C. 102(b) as being anticipated by Genshi et al., JP 63-022583.

Genshi et al., disclose compounds and composition thereof useful as germicide wherein, R1 is H, R4 is H or OH and R9 is CHO. See the abstract and compounds of formula I.

The compounds of Genshi et al., have limited number of variations for each substituent, there are no alternative points of attachments of the substituents to the rings and the parent structural nuclei do not change. Therefore, Genshi "has described to those of ordinary skill in [the] art each of the various permutations involved here as fully as if he had drawn each structural formula or had written each name." *In re Petering,* 133 USPQ 275 (CCPA 1962), *Bristol-Myers Squibs Co. v. Benvenue Labs. Inc.*, 246 F3d 1368, 1380 (Fed Cir, 2001).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5-6, 8, 10-19, 22-24, 26-29, 31-40, 43, 45-46, 48-49, 51, 53-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over the prior arts cited above, individually.

Applicant claims compounds of formula I their compositions and method of use for treating cancers, wherein R1, R4-R14 are aliphatic. In preferred embodiments they are lower alkyls or alkoxy.

Determination of the scope and content of the prior art (MPEP 2141.01)

Each prior art teaches similar compounds cited above wherein R1, R4-R14 are alkyls. Some teach them as lower alkoxy.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the instant invention and that of the prior arts is that the alkyl chain in applicant's compound is either shorter or longer than that of the prior arts. In other words applicant replaced H in the compounds of the prior arts with alkyl or vice versa.

Finding of prima facie obviousness---rational and motivation (MPEP 2142.2413)

However, H and alkyl are art recognized equivalents. *In re Lincoln*, 126 USPQ 477, 53 USPQ 40 (CCPA, 1942); *In re Druey*, 319 F.2d 237, 138 USPQ 39 (CCPA, 1963); *In re Lohr*, 317 F.2d 388, 137 USPQ 548 (CCPA, 1963); *In re Hoehsema*, 399 F.2d 269, 158 USPQ 598 (CCPA, 1968); *In re Wood*, 582 F.2d 638, 199 USPQ 137 (CCPA, 1978); *In re Hoke*, 560 F.2d 436, 195 USPQ 148 (CCPA, 1977); *Ex parte Fauque*, 121 USPQ 425 (POBA, 1954); *Ex parte Henkel*, 130 USPQ 474, (POBA, 1960).

When the difference between compounds is the length of a carbon chain such are adjacent homologs. However, adjacent homologs are prima facie obvious. *In re Henze*, 85 USPQ 261 (1950). Therefore, the instant invention is prima facie obvious from the teachings of the prior arts. One of ordinary skill in the art would have known to replace H with alkyl or vice versa at the time the invention was made. The motivation is from knowing that H and alkyl are equivalents and that adjacent homologs would have similar biochemical properties.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

TAOFIQ SOLOLA
PRIMARY EXAMINER
Group 1625

September 27, 2007